09/941,882

* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:36:34 ON 25 NOV 2003

=> file biosis medline caplus wpids uspatfull

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'BIOSIS' ENTERED AT 11:36:53 ON 25 NOV 2003
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FILE 'MEDLINE' ENTERED AT 11:36:53 ON 25 NOV 2003

FILE 'CAPLUS' ENTERED AT 11:36:53 ON 25 NOV 2003
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FILE 'WPIDS' ENTERED AT 11:36:53 ON 25 NOV 2003
COPYRIGHT (C) 2003 THOMSON DERWENT

FILE 'USPATFULL' ENTERED AT 11:36:53 ON 25 NOV 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

*** YOU HAVE NEW MAIL ***

=> s DNA sequencing
L1 52951 DNA SEQUENCING

=> s l1 and DNA polymerase (4a) reduc? (3a) exonuclease activity
L2 79 L1 AND DNA POLYMERASE (4A) REDUC? (3A) EXONUCLEASE ACTIVITY

=> s l2 and extension (10a) concentration? (10a) unincorporated deoxyribonucleotide?
L3 0 L2 AND EXTENSION (10A) CONCENTRATION? (10A) UNINCORPORATED DEOXYRIBONUCLEOTIDE?

=> s l2 and concentration? (13a) deoxyribonucleotide?
L4 6 L2 AND CONCENTRATION? (13A) DEOXYRIBONUCLEOTIDE?

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5 6 DUP REM L4 (0 DUPLICATES REMOVED)

=> d l5 bib abs 1-6

L5 ANSWER 1 OF 6 USPATFULL on STN
AN 2003:200824 USPATFULL
TI Method of determining the nucleotide sequence of oligonucleotides and DNA molecules
IN Williams, Peter, Phoenix, AZ, UNITED STATES
Hayes, Mark A., Chandler, AZ, UNITED STATES
Rose, Seth D., Tempe, AZ, UNITED STATES
Bloom, Linda B., Chandler, AZ, UNITED STATES
Reha-Krantz, Linda J., Edmonton, CANADA
Pizziconi, Vincent B., Phoenix, AZ, UNITED STATES
PI US 2003138809 A1 20030724
AI US 2002-229997 A1 20020828 (10)
RLI Continuation of Ser. No. US 2001-673544, filed on 26 Feb 2001, ABANDONED A 371 of International Ser. No. WO 1999-US9616, filed on 30 Apr 1999, PENDING
PRAI US 1998-83840P 19980501 (60)

09567863

DT Utility
FS APPLICATION
LREP BAKER & BOTTS, 30 ROCKEFELLER PLAZA, NEW YORK, NY, 10112
CLMN Number of Claims: 42
ECL Exemplary Claim: 1
DRWN 9 Drawing Page(s)
LN.CNT 1359
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a novel method for analyzing nucleic acid sequences based on real-time detection of DNA polymerase-catalyzed incorporation of each of the four nucleotide bases, supplied individually and serially in a microfluidic system, to a reaction cell containing a template system comprising a DNA fragment of unknown sequence and an oligonucleotide primer. Incorporation of a nucleotide base into the template system can be detected by any of a variety of methods including but not limited to fluorescence and chemiluminescence detection. Alternatively, microcalorimetic detection of the heat generated by the incorporation of a nucleotide into the extending template system using thermopile, thermistor and refractive index measurements can be used to detect extension reactions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 2 OF 6 USPATFULL on STN
AN 2002:251118 USPATFULL
TI Method of determining the nucleotide sequence of oligonucleotides and DNA molecules
IN Williams, Peter, Phoenix, AZ, UNITED STATES
Taylor, Thomas J., Tempe, AZ, UNITED STATES
Williams, Daniel J.B., Tempe, AZ, UNITED STATES
Gould, Ian, Phoenix, AZ, UNITED STATES
Hayes, Mark A., Gilbert, AZ, UNITED STATES
PI US 2002137062 A1 20020926
AI US 2001-941882 A1 20010828 (9)
RLI Continuation-in-part of Ser. No. US 2001-673544, filed on 26 Feb 2001, PENDING Continuation-in-part of Ser. No. WO 1999-US9616, filed on 30 Apr 1999, UNKNOWN
PRAI US 1998-83840P 19980501 (60)
DT Utility
FS APPLICATION
LREP BAKER & BOTTS, 30 ROCKEFELLER PLAZA, NEW YORK, NY, 10112
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 15 Drawing Page(s)
LN.CNT 2311
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a novel method for analyzing nucleic acid sequences based on real-time detection of DNA polymerase-catalyzed incorporation of each of the four nucleotide bases, supplied individually and serially in a microfluidic system, to a reaction cell containing a template system comprising a DNA fragment of unknown sequence and an oligonucleotide primer. Incorporation of a nucleotide base into the template system can be detected by any of a variety of methods including but not limited to fluorescence and chemiluminescence detection. Alternatively, microcalorimetic detection of the heat generated by the incorporation of a nucleotide into the extending template system using thermopile, thermistor and refractive index measurements can be used to detect extension reactions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 3 OF 6 USPATFULL on STN

09567863

AN 2002:78405 USPATFULL
TI Compositions and methods for analysis of nucleic acids
IN Makarov, Vladimir L., Ann Arbor, MI, UNITED STATES
Langmore, John P., Ann Arbor, MI, UNITED STATES
PA The Regents of the University of Michigan (U.S. corporation)
PI US 2002042059 A1 20020411
AI US 2001-801346 A1 20010306 (9)
RLI Continuation of Ser. No. US 1998-151236, filed on 10 Sep 1998, GRANTED, Pat. No. US 6197557 Continuation-in-part of Ser. No. US 1998-35677, filed on 5 Mar 1998, ABANDONED Continuation-in-part of Ser. No. US 1997-811804, filed on 6 Mar 1997, GRANTED, Pat. No. US 6117634
DT Utility
FS APPLICATION
LREP David L. Parker, FULBRIGHT & JAWORSKI L.L.P., 600 Congress Avenue, Suite 2400, Austin, TX, 78701
CLMN Number of Claims: 104
ECL Exemplary Claim: 1
DRWN 38 Drawing Page(s)
LN.CNT 6552
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are a number of methods that can be used in a variety of embodiments, including, creation of a nucleic acid terminated at one or more selected bases, sequence analysis of nucleic acids, mapping of sequence motifs within a nucleic acid, positional mapping of nucleic acid clones, and analysis of telomeric regions. The methods utilize double-stranded templates, and in most aspects involve a strand replacement reaction initiated at one or more random or specific locations created in a nucleic acid molecule, and in certain aspects utilizing an oligonucleotide primer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 4 OF 6 USPATFULL on STN
AN 2001:33054 USPATFULL
TI Compositions and methods for analysis of nucleic acids
IN Makarov, Vladimir L., Ann Arbor, MI, United States
Langmore, John P., Ann Arbor, MI, United States
PA The Regents of the University of Michigan, Ann Arbor, MI, United States (U.S. corporation)
PI US 6197557 B1 20010306
AI US 1998-151236 19980910 (9)
RLI Continuation-in-part of Ser. No. US 1998-35677, filed on 5 Mar 1998, now abandoned Continuation-in-part of Ser. No. US 1997-811804, filed on 6 Mar 1997, now patented, Pat. No. US 6117634
DT Utility
FS Granted
EXNAM Primary Examiner: Brusca, John S.; Assistant Examiner: Kim, Young
LREP Fulbright & Jaworski, LLP
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN 67 Drawing Figure(s); 38 Drawing Page(s)
LN.CNT 5768
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are a number of methods that can be used in a variety of embodiments, including, creation of a nucleic acid terminated at one or more selected bases, sequence analysis of nucleic acids, mapping of sequence motifs within a nucleic acid, positional mapping of nucleic acid clones, and analysis of telomeric regions. The methods utilize double-stranded templates, and in most aspects involve a strand replacement reaction initiated at one or more random or specific locations created in a nucleic acid molecule, and in certain aspects utilizing an oligonucleotide primer.

09567863

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 5 OF 6 USPATFULL on STN
AN 2000:77180 USPATFULL
TI Thermophilic DNA polymerases from Thermotoga neapolitana
IN Slater, Michael R., Madison, WI, United States
Huang, Fen, Madison, WI, United States
Hartnett, James R., Fitchburg, WI, United States
Bolchakova, Elena, Foster City, CA, United States
Storts, Douglas R., Madison, WI, United States
Otto, Paul, Madison, WI, United States
Miller, Katharine M., Verona, WI, United States
Novikov, Alexander, Foster City, CA, United States
Velikodvorskaya, Galina A., Moscow, Russian Federation
PA Promega Corporation, Madison, WI, United States (U.S. corporation)
PI US 6077664 20000620
AI US 1996-656664 19960531 (8)
RLI Continuation-in-part of Ser. No. US 1995-484661, filed on 7 Jun 1995, now patented, Pat. No. US 6001645
DT Utility
FS Granted
EXNAM Primary Examiner: Horlick, Kenneth R.
LREP Melden & Carroll, LLP.
CLMN Number of Claims: 48
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 7498
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to compositions of thermostable DNA polymerases derived from the hyperthermophilic eubacteria. In particular, the present invention comprises thermostable DNA polymerases from the hyperthermophilic eubacterium known as Thermotoga neapolitana. The present invention provides methods for utilizing naturally-occurring and non-naturally-occurring forms of T. neopolitana DNA polymerase. The T. neopolitana DNA polymerases of the present invention are used in combination with other compounds, including but not limited to pyrophosphatase and DNA polymerases from other thermophilic or hyperthermophilic organisms.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 6 OF 6 USPATFULL on STN
AN 1999:163500 USPATFULL
TI Thermophilic DNA polymerases from thermotoga neapolitana
IN Slater, Michael R., Madison, WI, United States
Huang, Fen, Madison, WI, United States
Hartnett, James R., Fitchburg, WI, United States
PA Promega Corporation, WI, United States (U.S. corporation)
PI US 6001645 19991214
AI US 1995-484661 19950607 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Sisson, Bradley; Assistant Examiner: Stole, Einar
LREP Medlen & Carroll, LLP
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 6586
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to thermostable DNA polymerases derived from the hyperthermophilic eubacteria, and Thermotoga neapolitana in

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particular. The present invention provides means for isolating and producing the enzymes from these thermostable DNA polymerases, which are useful in many recombinant DNA techniques, especially such techniques as thermal cycle sequencing and nucleic acid amplification.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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09567863

=> d his

(FILE 'HOME' ENTERED AT 11:36:34 ON 25 NOV 2003)

FILE 'BIOSIS, MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 11:36:53 ON 25 NOV 2003

L1 52951 S DNA SEQUENCING
L2 79 S L1 AND DNA POLYMERASE (4A) REDUC? (3A) EXONUCLEASE ACTIVITY
L3 0 S L2 AND EXTENSION (10A) CONCENTRATION? (10A) UNINCORPORATED D
L4 6 S L2 AND CONCENTRATION? (13A) DEOXYRIBONUCLEOTIDE?
L5 6 DUP REM L4 (0 DUPLICATES REMOVED)

=> s l2 and refractive index (4a) buffer
L6 3 L2 AND REFRACTIVE INDEX (4A) BUFFER

=> d l6 bib abs 1-3

L6 ANSWER 1 OF 3 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2000-052980 [04] WPIDS
CR 2003-278763 [27]
DNC C2000-013712
TI Novel method for determining the nucleotide sequence of DNA molecules.
DC B04 D16
IN BLOOM, L B; HAYES, M A; PIZZICONI, V B; REHA-KRANTZ, L J; ROSE, S D; WILLIAMS, P; GOULD, I; TAYLOR, T J; WILLIAMS, D J B
PA (UYAL-N) UNIV ALBERTA; (UYAR-N) UNIV ARIZONA STATE; (ARIZ-N) ARIZONA BOARD OF REGENTS; (GOUL-I) GOULD I; (HAYE-I) HAYES M A; (TAYL-I) TAYLOR T J; (WILL-I) WILLIAMS D J B; (WILL-I) WILLIAMS P; (BLOO-I) BLOOM L B; (PIZZ-I) PIZZICONI V B; (REHA-I) REHA-KRANTZ L J; (ROSE-I) ROSE S D
CYC 22
PI WO 9957321 A1 19991111 (200004)* EN 52p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
EP 1082458 A1 20010314 (200116) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002513594 W 20020514 (200236) 53p
US 2002137062 A1 20020926 (200265)
US 2003138809 A1 20030724 (200352)
ADT WO 9957321 A1 WO 1999-US9616 19990430; EP 1082458 A1 EP 1999-920270 19990430, WO 1999-US9616 19990430; JP 2002513594 W WO 1999-US9616 19990430, JP 2000-547272 19990430; US 2002137062 A1 Provisional US 1998-83840P 19980501, CIP of WO 1999-US9616 19990430, CIP of US 2001-673544 20010226, US 2001-941882 20010828; US 2003138809 A1 Provisional US 1998-83840P 19980501, Cont of WO 1999-US9616 19990430, Cont of US 2001-673544 20010226, US 2002-229997 20020828
FDT EP 1082458 A1 Based on WO 9957321; JP 2002513594 W Based on WO 9957321
PRAI US 1998-83840P 19980501; US 2001-673544 20010226; US 2001-941882 20010828; US 2002-229997 20020828
AN 2000-052980 [04] WPIDS
CR 2003-278763 [27]
AB WO 9957321 A UPAB: 20030813
NOVELTY - A novel method (A) of **DNA sequencing** based on real-time detection of DNA polymerase-catalyzed incorporation of each of the four nucleotide bases.
DETAILED DESCRIPTION - (A) comprises:
(a) providing (I) comprising at least one nucleic acid of unknown sequence hybridized to a primer oligonucleotide in the presence of a **DNA polymerase** with **reduced exonuclease activity**;
(b) contacting (I) with a single type of deoxyribonucleotide (II) under conditions which allow extension of the primer by incorporation of

at least one (II) to the 3' end of the primer to form an extended primer;
(c) detecting whether extension of the primer has occurred;
(d) detecting the number of (II) incorporated into the primer;
(e) removing unincorporated (II); and
(f) repeating steps (a) to (e) to determine the nucleotide sequence of the nucleic acid.

INDEPENDENT CLAIMS are also included for the following:

(1) a method of **DNA sequencing** comprises:
(a) providing a template system (I) comprising at least one nucleic acid molecule (NAM) of unknown sequence hybridized to a primer oligonucleotide in the presence of an exonuclease deficient DNA polymerase;
(b) contacting (I) with a single type of (II) under conditions which allow extension of the primer by incorporation of at least one (II) to the 3' end of the primer to form an extended primer;
(c) detecting whether extension of the primer has occurred, identifying the (II) added to the 3' end of the primer;
(d) detecting the number of (II) incorporated into the primer;
(e) removing unincorporated (II);
(f) contacting (I) with a mixture including an exonuclease proficient DNA polymerase, an exonuclease deficient DNA polymerase and the identified (II) of (b);
(g) removing the mixture of (f); and
(h) repeating steps (a) to (g) to determine the nucleotide sequence of the NAM;

(2) a method of **DNA sequencing** comprises:
(a) providing (I) comprising at least one NAM of unknown sequence hybridized to a primer oligonucleotide in the presence of a DNA polymerase;
(b) contacting (I) with a single type of (II) including a fluorescent moiety under conditions which allow extension of the primer by incorporation of a (II) to the 3' end of the primer to form an extended primer;
(c) removing unincorporated (II);
(d) detecting whether extension of the primer has occurred by removing the fluorescent moiety to a remote location and detecting the fluorescent moiety removed from the incorporated (II); and
(e) repeating steps (a) to (d) to determine the nucleotide sequence of the NAM;

(3) a test apparatus for **DNA sequencing**, including one or more of a plurality of elements including:
(a) a reaction chamber that incorporates a DNA template/primer system which produces a detectable signal when a DNA polymerase incorporates a deoxyribonucleotide monophosphate onto the 3' end of the primer strand;
(b) a means for introducing into, and evacuating from, the reaction chamber a plurality of reagents including, but not limited to, buffers, electrolytes, DNA template, DNA primer, deoxyribonucleotides and chemically modified deoxyribonucleotides and polymerase enzymes;
(c) a means for amplifying the signal; and
(d) a transduction element which transduces the signal into an electrical signal; and

(4) a test apparatus for DNA sequencing, including one or more of a plurality of elements including:
(a) a reaction chamber that incorporates a DNA template/primer system in which deoxyribonucleotide monophosphate may be caused to react with the DNA template/primer system in the presence of a DNA polymerase;
(b) a means for introducing into, and evacuating from, the reaction chamber reagents including, but not limited to, buffers, electrolytes, DNA template, DNA primer, deoxyribonucleotides and chemically modified deoxyribonucleotides and polymerase enzymes;
(c) a detection chamber in which one or more products of one or more chemical reactions in the reaction chamber are caused to generate a

detectable signal following a chemical reaction which incorporates one or more deoxyribonucleotides into the DNA template/primer system;

(d) a means for amplifying the signal; and

(e) a transduction element which transduces the signal into an electrical signal.

USE - The method can be used to determine the nucleotide sequence of genomic or cDNA fragments. It can also be used as a diagnostic tool for sequencing patient derived DNA samples.

ADVANTAGE - The invention provides a method for sequencing DNA that avoids electrophoretic separation of DNA fragments, thus eliminating the problems associated with anomalous migration of DNA due to repeated base sequences or other self-complementary sequences which can cause single stranded DNA to self-hybridize into hairpin loops. The method also avoids current limitations on the size of fragments that can be read. The effective cost of sequencing is also lowered, compared to prior art methods.

DESCRIPTION OF DRAWING(S) - The figure is a schematic diagram illustrating a reactive sequencing device containing a thin film bismuth antimony thermopile, in accordance with the invention.

Dwg.1/9

L6 ANSWER 2 OF 3 USPATFULL on STN
AN 2003:200824 USPATFULL
TI Method of determining the nucleotide sequence of oligonucleotides and DNA molecules
IN Williams, Peter, Phoenix, AZ, UNITED STATES
Hayes, Mark A., Chandler, AZ, UNITED STATES
Rose, Seth D., Tempe, AZ, UNITED STATES
Bloom, Linda B., Chandler, AZ, UNITED STATES
Reha-Krantz, Linda J., Edmonton, CANADA
Pizziconi, Vincent B., Phoenix, AZ, UNITED STATES
PI US 2003138809 A1 20030724
AI US 2002-229997 A1 20020828 (10)
RLI Continuation of Ser. No. US 2001-673544, filed on 26 Feb 2001, ABANDONED A 371 of International Ser. No. WO 1999-US9616, filed on 30 Apr 1999, PENDING
PRAI US 1998-83840P 19980501 (60)
DT Utility
FS APPLICATION
LREP BAKER & BOTTS, 30 ROCKEFELLER PLAZA, NEW YORK, NY, 10112
CLMN Number of Claims: 42
ECL Exemplary Claim: 1
DRWN 9 Drawing Page(s)
LN.CNT 1359
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a novel method for analyzing nucleic acid sequences based on real-time detection of DNA polymerase-catalyzed incorporation of each of the four nucleotide bases, supplied individually and serially in a microfluidic system, to a reaction cell containing a template system comprising a DNA fragment of unknown sequence and an oligonucleotide primer. Incorporation of a nucleotide base into the template system can be detected by any of a variety of methods including but not limited to fluorescence and chemiluminescence detection. Alternatively, microcalorimetic detection of the heat generated by the incorporation of a nucleotide into the extending template system using thermopile, thermistor and refractive index measurements can be used to detect extension reactions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 3 OF 3 USPATFULL on STN
AN 2002:251118 USPATFULL

09567863

TI Method of determining the nucleotide sequence of oligonucleotides and DNA molecules
IN Williams, Peter, Phoenix, AZ, UNITED STATES
Taylor, Thomas J., Tempe, AZ, UNITED STATES
Williams, Daniel J.B., Tempe, AZ, UNITED STATES
Gould, Ian, Phoenix, AZ, UNITED STATES
Hayes, Mark A., Gilbert, AZ, UNITED STATES
PI US 2002137062 A1 20020926
AI US 2001-941882 A1 20010828 (9)
RLI Continuation-in-part of Ser. No. US 2001-673544, filed on 26 Feb 2001, PENDING Continuation-in-part of Ser. No. WO 1999-US9616, filed on 30 Apr 1999, UNKNOWN
PRAI US 1998-83840P 19980501 (60)
DT Utility
FS APPLICATION
LREP BAKER & BOTTS, 30 ROCKEFELLER PLAZA, NEW YORK, NY, 10112
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 15 Drawing Page(s)
LN.CNT 2311
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a novel method for analyzing nucleic acid sequences based on real-time detection of DNA polymerase-catalyzed incorporation of each of the four nucleotide bases, supplied individually and serially in a microfluidic system, to a reaction cell containing a template system comprising a DNA fragment of unknown sequence and an oligonucleotide primer. Incorporation of a nucleotide base into the template system can be detected by any of a variety of methods including but not limited to fluorescence and chemiluminescence detection. Alternatively, microcalorimetic detection of the heat generated by the incorporation of a nucleotide into the extending template system using thermopile, thermistor and refractive index measurements can be used to detect extension reactions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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=> d his

(FILE 'HOME' ENTERED AT 11:36:34 ON 25 NOV 2003)

FILE 'BIOSIS, MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 11:36:53 ON 25 NOV 2003
L1 52951 S DNA SEQUENCING
L2 79 S L1 AND DNA POLYMERASE (4A) REDUC? (3A) EXONUCLEASE ACTIVITY
L3 0 S L2 AND EXTENSION (10A) CONCENTRATION? (10A) UNINCORPORATED D
L4 6 S L2 AND CONCENTRATION? (13A) DEOXYRIBONUCLEOTIDE?
L5 6 DUP REM L4 (0 DUPLICATES REMOVED)
L6 3 S L2 AND REFRACTIVE INDEX (4A) BUFFER
L7 2 S L2 AND PYROPHOSPHATE (4A) RELEASE

=> s l7 and heat
L8 2 L7 AND HEAT

=> d l8 bib abs 1-2

L8 ANSWER 1 OF 2 USPATFULL on STN
AN 2002:78405 USPATFULL
TI Compositions and methods for analysis of nucleic acids
IN Makarov, Vladimir L., Ann Arbor, MI, UNITED STATES
Langmore, John P., Ann Arbor, MI, UNITED STATES
PA The Regents of the University of Michigan (U.S. corporation)
PI US 2002042059 A1 20020411
AI US 2001-801346 A1 20010306 (9)
RLI Continuation of Ser. No. US 1998-151236, filed on 10 Sep 1998, GRANTED, Pat. No. US 6197557 Continuation-in-part of Ser. No. US 1998-35677, filed on 5 Mar 1998, ABANDONED Continuation-in-part of Ser. No. US 1997-811804, filed on 6 Mar 1997, GRANTED, Pat. No. US 6117634
DT Utility
FS APPLICATION
LREP David L. Parker, FULBRIGHT & JAWORSKI L.L.P., 600 Congress Avenue, Suite 2400, Austin, TX, 78701
CLMN Number of Claims: 104
ECL Exemplary Claim: 1
DRWN 38 Drawing Page(s)
LN.CNT 6552
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are a number of methods that can be used in a variety of embodiments, including, creation of a nucleic acid terminated at one or more selected bases, sequence analysis of nucleic acids, mapping of sequence motifs within a nucleic acid, positional mapping of nucleic acid clones, and analysis of telomeric regions. The methods utilize double-stranded templates, and in most aspects involve a strand replacement reaction initiated at one or more random or specific locations created in a nucleic acid molecule, and in certain aspects utilizing an oligonucleotide primer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 2 OF 2 USPATFULL on STN
AN 2001:33054 USPATFULL
TI Compositions and methods for analysis of nucleic acids
IN Makarov, Vladimir L., Ann Arbor, MI, United States
Langmore, John P., Ann Arbor, MI, United States
PA The Regents of the University of Michigan, Ann Arbor, MI, United States (U.S. corporation)
PI US 6197557 B1 20010306
AI US 1998-151236 19980910 (9)

09567863

RLI Continuation-in-part of Ser. No. US 1998-35677, filed on 5 Mar 1998, now abandoned Continuation-in-part of Ser. No. US 1997-811804, filed on 6 Mar 1997, now patented, Pat. No. US 6117634
DT Utility
FS Granted
EXNAM Primary Examiner: Brusca, John S.; Assistant Examiner: Kim, Young
LREP Fulbright & Jaworski, LLP
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN 67 Drawing Figure(s); 38 Drawing Page(s)
LN.CNT 5768
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are a number of methods that can be used in a variety of embodiments, including, creation of a nucleic acid terminated at one or more selected bases, sequence analysis of nucleic acids, mapping of sequence motifs within a nucleic acid, positional mapping of nucleic acid clones, and analysis of telomeric regions. The methods utilize double-stranded templates, and in most aspects involve a strand replacement reaction initiated at one or more random or specific locations created in a nucleic acid molecule, and in certain aspects utilizing an oligonucleotide primer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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=> d l9 bib abs 1-3

L9 ANSWER 1 OF 3 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2000-052980 [04] WPIDS
CR 2003-278763 [27]
DNC C2000-013712
TI Novel method for determining the nucleotide sequence of DNA molecules.
DC B04 D16
IN BLOOM, L B; HAYES, M A; PIZZICONI, V B; REHA-KRANTZ, L J; ROSE, S D; WILLIAMS, P; GOULD, I; TAYLOR, T J; WILLIAMS, D J B
PA (UYAL-N) UNIV ALBERTA; (UYAR-N) UNIV ARIZONA STATE; (ARIZ-N) ARIZONA BOARD OF REGENTS; (GOUL-I) GOULD I; (HAYE-I) HAYES M A; (TAYL-I) TAYLOR T J; (WILL-I) WILLIAMS D J B; (WILL-I) WILLIAMS P; (BLOO-I) BLOOM L B; (PIZZ-I) PIZZICONI V B; (REHA-I) REHA-KRANTZ L J; (ROSE-I) ROSE S D
CYC 22
PI WO 9957321 A1 19991111 (200004)* EN 52p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
EP 1082458 A1 20010314 (200116) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002513594 W 20020514 (200236) 53p
US 2002137062 A1 20020926 (200265)
US 2003138809 A1 20030724 (200352)
ADT WO 9957321 A1 WO 1999-US9616 19990430; EP 1082458 A1 EP 1999-920270 19990430, WO 1999-US9616 19990430; JP 2002513594 W WO 1999-US9616 19990430, JP 2000-547272 19990430; US 2002137062 A1 Provisional US 1998-83840P 19980501, CIP of WO 1999-US9616 19990430, CIP of US 2001-673544 20010226, US 2001-941882 20010828; US 2003138809 A1 Provisional US 1998-83840P 19980501, Cont of WO 1999-US9616 19990430, Cont of US 2001-673544 20010226, US 2002-229997 20020828
FDT EP 1082458 A1 Based on WO 9957321; JP 2002513594 W Based on WO 9957321
PRAI US 1998-83840P 19980501; US 2001-673544 20010226; US 2001-941882 20010828; US 2002-229997 20020828
AN 2000-052980 [04] WPIDS
CR 2003-278763 [27]
AB WO 9957321 A UPAB: 20030813
NOVELTY - A novel method (A) of **DNA sequencing** based on real-time detection of DNA polymerase-catalyzed incorporation of each of the four nucleotide bases.

DETAILED DESCRIPTION - (A) comprises:

(a) providing (I) comprising at least one nucleic acid of unknown sequence hybridized to a primer oligonucleotide in the presence of a **DNA polymerase** with **reduced exonuclease activity**;

(b) contacting (I) with a single type of deoxyribonucleotide (II) under conditions which allow extension of the primer by incorporation of at least one (II) to the 3' end of the primer to form an extended primer;

(c) detecting whether extension of the primer has occurred;

(d) detecting the number of (II) incorporated into the primer;

(e) removing unincorporated (II); and

(f) repeating steps (a) to (e) to determine the nucleotide sequence of the nucleic acid.

INDEPENDENT CLAIMS are also included for the following:

(1) a method of **DNA sequencing** comprises:

(a) providing a template system (I) comprising at least one nucleic acid molecule (NAM) of unknown sequence hybridized to a primer oligonucleotide in the presence of an exonuclease deficient DNA polymerase;

(b) contacting (I) with a single type of (II) under conditions which allow extension of the primer by incorporation of at least one (II) to the 3' end of the primer to form an extended primer;

(c) detecting whether extension of the primer has occurred, identifying the (II) added to the 3' end of the primer;
(d) detecting the number of (II) incorporated into the primer;
(e) removing unincorporated (II);
(f) contacting (I) with a mixture including an exonuclease proficient DNA polymerase, an exonuclease deficient DNA polymerase and the identified (II) of (b);
(g) removing the mixture of (f); and
(h) repeating steps (a) to (g) to determine the nucleotide sequence of the NAM;
(2) a method of **DNA sequencing** comprises:
(a) providing (I) comprising at least one NAM of unknown sequence hybridized to a primer oligonucleotide in the presence of a DNA polymerase;
(b) contacting (I) with a single type of (II) including a fluorescent moiety under conditions which allow extension of the primer by incorporation of a (II) to the 3' end of the primer to form an extended primer;
(c) removing unincorporated (II);
(d) detecting whether extension of the primer has occurred by removing the fluorescent moiety to a remote location and detecting the fluorescent moiety removed from the incorporated (II); and
(e) repeating steps (a) to (d) to determine the nucleotide sequence of the NAM;
(3) a test apparatus for **DNA sequencing**, including one or more of a plurality of elements including:
(a) a reaction chamber that incorporates a DNA template/primer system which produces a detectable signal when a DNA polymerase incorporates a deoxyribonucleotide monophosphate onto the 3' end of the primer strand;
(b) a means for introducing into, and evacuating from, the reaction chamber a plurality of reagents including, but not limited to, buffers, electrolytes, DNA template, DNA primer, deoxyribonucleotides and chemically modified deoxyribonucleotides and polymerase enzymes;
(c) a means for amplifying the signal; and
(d) a transduction element which transduces the signal into an electrical signal; and
(4) a test apparatus for DNA sequencing, including one or more of a plurality of elements including:
(a) a reaction chamber that incorporates a DNA template/primer system in which deoxyribonucleotide monophosphate may be caused to react with the DNA template/primer system in the presence of a DNA polymerase;
(b) a means for introducing into, and evacuating from, the reaction chamber reagents including, but not limited to, buffers, electrolytes, DNA template, DNA primer, deoxyribonucleotides and chemically modified deoxyribonucleotides and polymerase enzymes;
(c) a detection chamber in which one or more products of one or more chemical reactions in the reaction chamber are caused to generate a detectable signal following a chemical reaction which incorporates one or more deoxyribonucleotides into the DNA template/primer system;
(d) a means for amplifying the signal; and
(e) a transduction element which transduces the signal into an electrical signal.

USE - The method can be used to determine the nucleotide sequence of genomic or cDNA fragments. It can also be used as a diagnostic tool for sequencing patient derived DNA samples.

ADVANTAGE - The invention provides a method for sequencing DNA that avoids electrophoretic separation of DNA fragments, thus eliminating the problems associated with anomalous migration of DNA due to repeated base sequences or other self-complementary sequences which can cause single stranded DNA to self-hybridize into hairpin loops. The method also avoids current limitations on the size of fragments that can be read. The effective cost of sequencing is also lowered, compared to prior art

methods.

DESCRIPTION OF DRAWING(S) - The figure is a schematic diagram illustrating a reactive sequencing device containing a thin film bismuth antimony thermopile, in accordance with the invention.

Dwg.1/9

L9 ANSWER 2 OF 3 USPATFULL on STN
AN 2003:200824 USPATFULL
TI Method of determining the nucleotide sequence of oligonucleotides and DNA molecules
IN Williams, Peter, Phoenix, AZ, UNITED STATES
Hayes, Mark A., Chandler, AZ, UNITED STATES
Rose, Seth D., Tempe, AZ, UNITED STATES
Bloom, Linda B., Chandler, AZ, UNITED STATES
Reha-Krantz, Linda J., Edmonton, CANADA
Pizziconi, Vincent B., Phoenix, AZ, UNITED STATES
PI US 2003138809 A1 20030724
AI US 2002-229997 A1 20020828 (10)
RLI Continuation of Ser. No. US 2001-673544, filed on 26 Feb 2001, ABANDONED A 371 of International Ser. No. WO 1999-US9616, filed on 30 Apr 1999, PENDING
PRAI US 1998-83840P 19980501 (60)
DT Utility
FS APPLICATION
LREP BAKER & BOTTS, 30 ROCKEFELLER PLAZA, NEW YORK, NY, 10112
CLMN Number of Claims: 42
ECL Exemplary Claim: 1
DRWN 9 Drawing Page(s)
LN.CNT 1359
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a novel method for analyzing nucleic acid sequences based on real-time detection of DNA polymerase-catalyzed incorporation of each of the four nucleotide bases, supplied individually and serially in a microfluidic system, to a reaction cell containing a template system comprising a DNA fragment of unknown sequence and an oligonucleotide primer. Incorporation of a nucleotide base into the template system can be detected by any of a variety of methods including but not limited to fluorescence and chemiluminescence detection. Alternatively, microcalorimetic **detection** of the **heat generated** by the incorporation of a nucleotide into the extending template system using thermopile, thermistor and refractive index measurements can be used to detect extension reactions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 3 OF 3 USPATFULL on STN
AN 2002:251118 USPATFULL
TI Method of determining the nucleotide sequence of oligonucleotides and DNA molecules
IN Williams, Peter, Phoenix, AZ, UNITED STATES
Taylor, Thomas J., Tempe, AZ, UNITED STATES
Williams, Daniel J.B., Tempe, AZ, UNITED STATES
Gould, Ian, Phoenix, AZ, UNITED STATES
Hayes, Mark A., Gilbert, AZ, UNITED STATES
PI US 2002137062 A1 20020926
AI US 2001-941882 A1 20010828 (9)
RLI Continuation-in-part of Ser. No. US 2001-673544, filed on 26 Feb 2001, PENDING Continuation-in-part of Ser. No. WO 1999-US9616, filed on 30 Apr 1999, UNKNOWN
PRAI US 1998-83840P 19980501 (60)
DT Utility
FS APPLICATION

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CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 15 Drawing Page(s)
LN.CNT 2311
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a novel method for analyzing nucleic acid sequences based on real-time detection of DNA polymerase-catalyzed incorporation of each of the four nucleotide bases, supplied individually and serially in a microfluidic system, to a reaction cell containing a template system comprising a DNA fragment of unknown sequence and an oligonucleotide primer. Incorporation of a nucleotide base into the template system can be detected by any of a variety of methods including but not limited to fluorescence and chemiluminescence detection. Alternatively, microcalorimetic **detection** of the **heat generated** by the incorporation of a nucleotide into the extending template system using thermopile, thermistor and refractive index measurements can be used to detect extension reactions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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